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Acromegaly and Hyperthyroidism Associated with McCune-Albright Syndrome

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Abstract. A 36-year-old man is described having McCune-Albright syndrome, acromegaly likely due to somatotroph hyperplasia and hyperthyroidism due to adenomatous goiter. Sexual precocity was not noted. The sella was narrow in size and no mass was seen. The decline of elevated GH by hyperglycemia and increase by GHRH-44(NH_2) may support somatotroph hyperplasia, but plasma GHRH-44(NH_2) levels were not elevated. A mass in the right lobe and enlargement of the left lobe of the thyroid were noted. Thyroid hormone levels in serum and thyroidal radioiodine uptake values were elevated, while TSH measurements in serum were low. The radioiodine scan showed a cold nodule in the right lobe and a hot area in the left of the thyroid. Thyroidal radioiodine was not suppressed following T_3 given orally. These findings are compatible with functioning glands autonomously as the mechanism for the endocrinopathies associated with the McCune-Albright syndrome.

Introduction

McCune-Albright syndrome consists of the triad of polyostotic fibrous dysplasia of bone, hyperpigmented skin macules, and a wide variety of endocrinopathies including isosexual precocity, hyperthyroidism, Cushing's syndrome, hyperparathyroidism and acromegaly [1]. The etiology of the endocrinopathies is obscure. DiGeorge [2] proposed that it may be a form of multiple endocrine adenomatosis.

We describe here a man having McCune-Albright syndrome, acromegaly likely due to somatotroph hyperplasia and hyperthyroidism due to adenomatous goiter.

Case Report

A 36-year-old man was referred in October 1984 for evaluation of his goiter. The goiter, first noted in 1976, had enlarged gradually. He had lost 7 kg for about 6 months but denied anorexia. He had complained of nervousness, fatigue and intolerance to heat. Sexual precocity was not noted and puberty had developed normally. On examination, he was 172 cm in height and 57.5 kg in weight. The head was disproportionately large with frontal bossing and parietal prominences. Café-au-lait pigmentation with irregular borders was noted on the chin. He showed a slight tremor of the hands. The skin was moist. There was no exophthalmos and no stare. A 4 × 5 cm mass in the right lobe and enlargement of the left lobe of the thyroid were noted. The supine blood pressure was 138/64 mm Hg, pulse 68/min and regular. Visual fields and fundi were normal. Neurological examinations were negative except for left hearing impairment.

A diagnosis of adenomatous goiter with hyperthyroidism was made. Thyroid studies included a serum T_4 of 17.9 μg/dl (normal 6.0–12.0 μg/dl), T_3 of 196 ng/dl (normal 90–180 ng/dl), TSH of 1.1 μU/ml (normal < 8 μU/ml) and ^{123}I thyroid uptake of 40.7% of 24 h. TRH did not stimulate TSH release. Tests for thyrotropin binding inhibitory immunoglobulin, antithyroglobulin and antimicrosomal antibodies were negative. The radioiodine scan showed a cold nodule in the right lobe and a hot area in the left of the thyroid. Thyroidal radioiodine was not suppressed following 75 μg of T_3 given orally for 7 days. The cold nodule in the right lobe was cystic by aspiration biopsy. The hyperthyroidism had been controlled with antithyroid medication.

A diagnosis of acromegaly was made. Basal serum GH levels (9 samples) were modestly elevated and fluctuated between 13 and 24 ng/ml. Plasma somatomedin-C level was 3.2 U/ml (normal 0.36–2.00 U/ml). Serum GH decreased after 75 g oral glucose administration from 20 to 10 ng/ml at 30 min and increased after *L*-arginine administration (30 g i.v. infusion) from 14 to 48 ng/ml at 60 min. Neither TRH (500 μg i.v.) nor LHRH (100 μg i.v.) increased serum GH levels. Serum GH increased from 14 to 36 ng/ml at 60 min in response to 100 μg of synthetic human pancreatic GHRH-44(NH_2) bolus injection. Serum GH did not change after 2.5 mg oral bromocriptine administration. Plasma GHRH levels were measured by the RIA method [3]. Plasma GHRH levels were 5 pg/ml (normal 3.9–

11.7 pg/ml). Serum PRL levels were not affected by administration of TRH, but decreased from 59 to 5.6 ng/ml 6 h after bromocriptine administration. Serum LH and FSH were increased from 10.2 and 16.1 mIU/ml to 175.2 and 64.2 mIU/ml, respectively, at 60 min in response to LHRH bolus injection. Morning plasma ACTH and cortisol levels were 54 pg/ml (normal 10–100 pg/ml) and 11.3 μg/dl (normal 3.7–13.0 μg/dl), respectively.

X-rays of the skull showed irregular thickening of the base and of the cranium with numerous cystic-appearing areas. Cranial lesions were biopsied and found to be fibrous dysplasia. The sella was narrow in size and no mass was seen in CT. ^{99}Tc bone scintigram showed abnormal accumulation in the skull and left clavicula. A neurosurgical consultation was obtained and it was decided that a surgical approach would be difficult owing to the severe thickening of the cranium and sphenoid bone by the fibrous dysplasia.

Discussion

The etiology of the various endocrinopathies associated with the McCune-Albright syndrome is poorly understood. According to several workers, pituitary overactivity in patients with the McCune-Albright syndrome were secondary to constant stimulating of pituitary cells either through deficiency of hypothalamic inhibitory hormones or through excess of hypothalamic releasing hormones [4]. On the other hand, it has been proposed that the pituitary lesion represents a primary autonomous disorder which develops unrelated to the hypothalamus [2]. This may represent a form of the multiple endocrine adenomatous syndrome.

This patient had polyostotic fibrous dysplasia, skin pigmentation, acromegaly and hyperthyroidism. Firat and Stutzman [5] described a similar case of a 21-year-old man. Pathologic examination of the gland revealed multiple adenomas of the thyroid gland. Abnormalities of the thyroid, particular goiters and hyperthyroidism are the secondmost common form of endocrinopathy in the McCune-Albright syndrome [6]. Hamilton and Maloof [7] have reviewed hyperthyroidism of the McCune-Albright syndrome. Ten of their 16 patients had goiters which were multinodular by palpation or adenomatous by pathological examination (4 males and 6 females). The average age of their patients with toxic multinodular goiter was 22.9 years. In the present case, baseline TSH was low and there was no response to TRH. This patient had a hyperthyroidism due to clinically adenomatous goiter. The mechanism for development of hyperthyroidism is not known, but the thyroid appears to be functioning autonomously. His second endocrinologic abnormality, acromegaly, is encountered rarely in McCune-Albright syndrome. The few reported histologic studies in the adenohypophyses describe eosinophilic adenoma [8], multiloculated chromophobe adenoma [9] and multifocal acidophilic cell hyperplasia [10]. In this patient, neither tomography nor CT of the head could detect pituitary mass, suggesting that the hypersecretion of GH is caused by long-standing hypothalamic stimuli which may induce the release of GHRH rather than a rapidly growing pituitary tumor. The responses of serum GH to changes in serum glucose concentrations suggest that the pituitary response is controlled by hypothalamic stimuli [11], but plasma GHRH values were normal. Explanation based on the theory of increased pituitary sensitivity to GHRH is also likely. Somatotroph hyperplasia was supported by laboratory data indicating of exaggerated response to GHRH. Whether, in our patient, somatotroph hyperplasia represented a adenomatous condition remains unresolved.

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